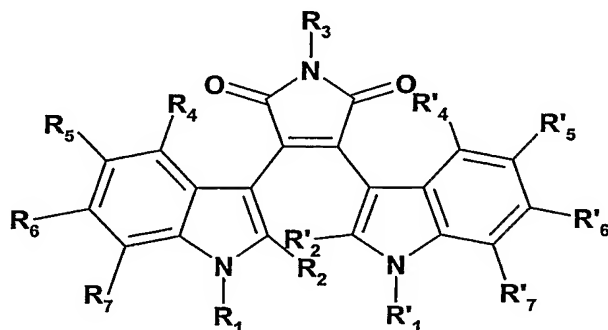


CLAIMS

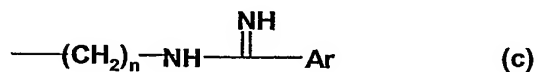
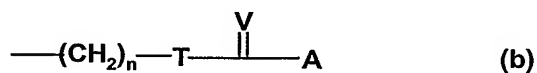
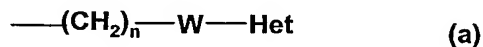
1. Use of a protein kinase C inhibitor of formula I, II, III or IV or a pharmaceutically acceptable salt, hydrate or solvate thereof in the preparation of a pharmaceutical composition for the treatment and prevention of autoimmune diseases,

wherein compounds of formula I are



wherein

each of R_1 and R'_1 , independently, is hydrogen, alkyl, haloalkyl, alkenyl, arylalkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, acylaminoalkyl, acyloxyalkyl, cyanoalkyl, amidinoalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, or a group of the formula (a), (b) or (c)



wherein Het signifies a heterocyclyl group; W signifies NH, S or a bond; T signifies NH or S; V signifies O, S, NH, or NCN; A signifies alkylthio, amino, monoalkylamino or dialkylamino; Ar signifies aryl;

each of R_2 and R'_2 , independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, $\text{C}_1\text{---C}_3$ alkylthio, $\text{S(O)C}_1\text{---C}_3$ alkyl, CF_3 ;

or R_1 and R_2 form together $\text{---}(\text{CH}_2)_r\text{---X---CH}_2\text{---}$ wherein r is 1, 2, or 3, and X is CHR_8 or NR_8 wherein R_8 is $(\text{CH}_2)_s\text{R}_9$ wherein R_9 is hydrogen, hydroxy, alkoxy, amino,

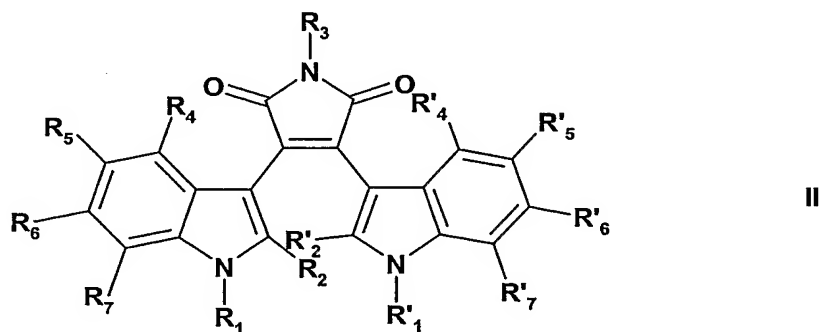
monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and *s* is 0, 1, 2 or 3;

R_3 is hydrogen or CH_3CO ;

each of R_4 , R'_4 , R_5 , R'_5 , R_6 , R'_6 , R_7 and R'_7 , independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, $-\text{COO}(\text{C}_1-\text{C}_3\text{alkyl})$, CF_3 , nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, $\text{C}_1-\text{C}_3\text{alkylthio}$, or $\text{S}(\text{O})\text{C}_1-\text{C}_3\text{alkyl}$; and

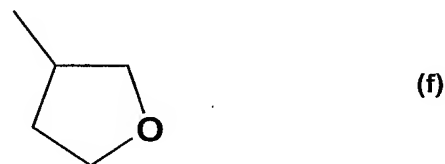
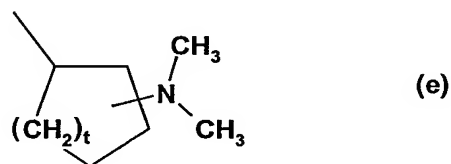
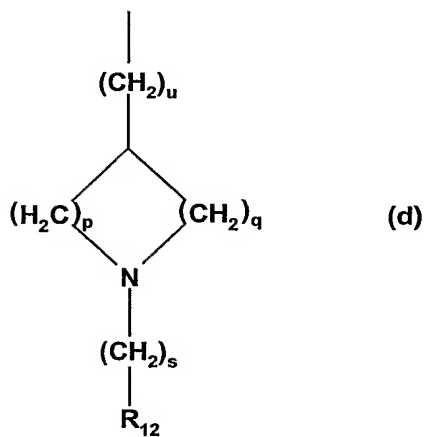
n is 1, 2, 3, 4, 5 or 6;

and compounds of formula II are



wherein

R_1 is a group of formula (d), (e) or (f)



wherein each of *p* and *q* independently is 1, 2, 3, or 4;

s is 0, 1, 2 or 3;

t is 1 or 2;

u is 0 or 1; and

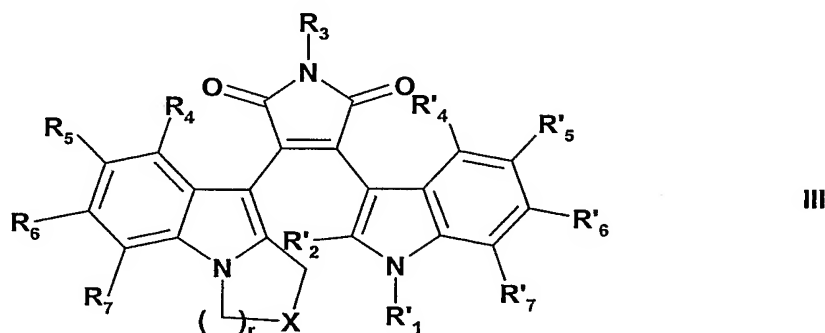
R_{12} is hydrogen, alkyl, haloalkyl, cycloalkyl, acetyl, aryl, $-\text{CH}(\text{aryl})_2$, amino, monoalkylamino, dialkylamino, guanidino, $-\text{C}(=\text{N}(\text{alkoxycarbonyl}))\text{NH}(\text{alkoxy-carbonyl})$, amidino, hydroxy, carboxy, alkoxycarbonyl or heterocyclyl;

R'_1 is hydrogen, C_{1-4} alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl, each of R_2 and R'_2 , independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3 alkylthio, $\text{S}(\text{O})\text{C}_1-\text{C}_3$ alkyl, CF_3 ;

R_3 is hydrogen or $\text{CH}_3\text{CO}-$; and

each of R_4 , R'_4 , R_5 , R'_5 , R_6 , R'_6 , R_7 and R'_7 , independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, $-\text{COO}(\text{C}_1-\text{C}_3\text{alkyl})$, CF_3 , nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3 alkylthio, or $\text{S}(\text{O})\text{C}_1-\text{C}_3$ alkyl;

and compounds of formula III are



wherein

R'_1 is hydrogen, C_1-C_4 alkyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl;

R'_2 is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, C_1-C_3 alkylthio, $\text{S}(\text{O})\text{C}_1-\text{C}_3$ alkyl, CF_3

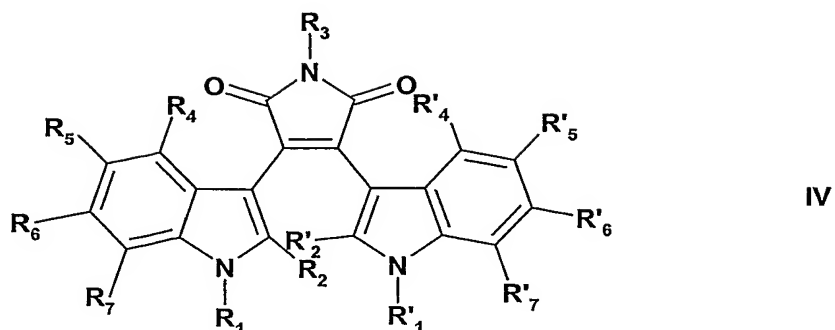
R_3 is hydrogen or $\text{CH}_3\text{CO}-$;

each of R_4 , R'_4 , R_5 , R'_5 , R_6 , R'_6 , R_7 and R'_7 , independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, $-\text{COO}(\text{C}_1-\text{C}_3\text{alkyl})$, CF_3 , nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, C_1-C_3 alkylthio, or $\text{S}(\text{O})\text{C}_1-\text{C}_3$ alkyl;

X is CR_8R_9 wherein R_8 is $(\text{CH}_2)_s\text{R}_{10}$ wherein R_9 is $(\text{CH}_2)_s\text{R}_{11}$, each of R_{10} and R_{11} , independently, is hydroxy, alkoxy, carboxy, acyloxy, amino, monoalkylamino, dialkylamino, trialkylamino, azido, acylamino, alkoxycarbonyl, cyano, amidino, or aminocarbonyl, and s is 0, 1, 2 or 3; and

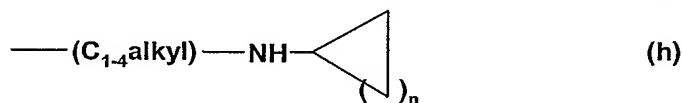
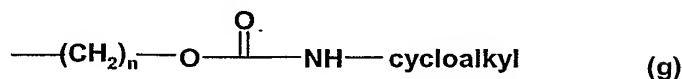
r is 1, 2, or 3; and

and compounds of formula IV are



wherein

R_1 is alkylglycoside residue or a group of formula (g) or (h)



wherein n is 1, 2, 3, 4, 5 or 6;

R'_1 is hydrogen, $\text{C}_1\text{--C}_4$ alkyl, cyclopropylmethyl, aminoalkyl, monoalkylaminoalkyl, or dialkylaminoalkyl;

each of R_2 and R'_2 , independently, is hydrogen, alkyl, alkoxyalkyl, hydroxyalkyl, $\text{C}_1\text{--C}_3$ alkylthio, $\text{S}(\text{O})\text{C}_1\text{--C}_3$ alkyl, CF_3 ;

R_3 is hydrogen or $\text{CH}_3\text{CO--}$; and

each of R_4 , R'_4 , R_5 , R'_5 , R_6 , R'_6 , R_7 and R'_7 , independently, is hydrogen, halogen, alkyl, hydroxy, alkoxy, $\text{--COO}(\text{C}_1\text{--C}_3\text{alkyl})$, CF_3 , nitro, amino, acetylamino, monoalkylamino, dialkylamino, alkylthio, $\text{C}_1\text{--C}_3$ alkylthio, or $\text{S}(\text{O})\text{C}_1\text{--C}_3$ alkyl.

2. Use according to claim 1 wherein the autoimmune diseases are selected from inflammatory bowel diseases e.g. Crohn's disease and ulcerative colitis; amyotrophic lateral sclerosis; multiple sclerosis; rheumatoid arthritis and hepatitis C.
3. Use of a protein kinase C inhibitor of formula I, II, III or IV according to claim 1, or a pharmaceutically acceptable salt, hydrate or solvate thereof in the preparation of a pharmaceutical composition for the treatment and prevention of organ or tissue transplant rejection and for the prevention of graft-versus-host disease.
4. Use according to any one of claims 1 to 3 wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.

5. Use according to any one of claims 1 to 3 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-((1-pyridin-2-ylmethyl)-piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.
6. A pharmaceutical composition for use in the treatment and prevention of organ or tissue transplant rejection and for the prevention of graft-versus-host disease and/or of autoimmune diseases comprising a protein kinase C inhibitor of formula I, II, III or IV or a pharmaceutically acceptable salt, hydrate or solvate thereof, together with one or more pharmaceutically acceptable diluents or carriers therefor.
7. Composition according to claim 6 wherein the protein kinase C inhibitor is a compound of formula Ia, Ib, IIa, IIIa or a pharmaceutically acceptable salt, hydrate or solvate thereof.
8. Composition according to claim 6 wherein the protein kinase C inhibitor is 3-(1-methyl-1H-indol-3-yl)-4-[1-((1-pyridin-2-ylmethyl)-piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.
9. A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula I, II, III or IV, or a pharmaceutically acceptable salt, hydrate or solvate thereof, and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.
10. A pharmaceutical combination comprising a) a protein kinase C inhibitor of formula Ia, Ib, IIa, or IIIa, e.g. 3-(1-methyl-1H-indol-3-yl)-4-[1-((1-pyridin-2-ylmethyl)-piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof and b) at least one second agent selected from an immunosuppressant and immunomodulatory drug.
11. A method for treating or preventing organ or tissue transplant rejection or an autoimmune disease or for preventing graft-versus-host disease in a subject in need thereof, comprising administering to said subject a therapeutically effective amount of a protein kinase C inhibitor of formula I, II, III or IV, e.g. a compound of formula Ia, Ib, IIa, IIIa, preferably 3-(1-methyl-1H-indol-3-yl)-4-[1-((1-pyridin-2-ylmethyl)-piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione or 3-(1-methyl-1H-indol-3-yl)-4-[1-(piperidin-4-yl)-1H-indol-3-yl]-pyrrole-2,5-dione, or a pharmaceutically acceptable salt, hydrate or solvate thereof.